FDA U.S. Food and Drug Administration Department of Health and Human Services

# Food and Drug Administration Activities and Interests Related to SARS

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# SARS: The FDA Focus

- **Encourage & Facilitate Needed Product Development:**
  - Development of Rapid Diagnostic Tests
  - Development of Vaccine
  - Development of Therapeutic Drugs and Biologics
- **Protect the Safety of the Blood Supply**
- **Assure Adequacy of U.S. Medical Supplies in the Event of a Large SARS Outbreak in the U.S.**

# Facilitate Development of Rapid Diagnostics

- CDRH worked with CDC on IDE for prototype PCR
- Working with private sector on their development projects
- Secretary, Commissioner and CDRH and CBER Directors met early with major diagnostic companies' senior business and scientific officers to encourage development and registration of a rapid diagnostic that could be used in local hospitals/physician offices and of technologies useful for blood screening, were it to be required
- Had open, public meeting on diagnostics patterned on WNV response: methods, standards, clinical indications, identifying scientific and technologic challenges
  - FDA work with CDC and others to facilitate sample sharing

# Support Vaccine Development

- Working with private sector and NIH on their early activities, including CBER/CDC joint facilitation of availability of appropriate GLP laboratory isolates for seed stock
- Secretary, Commissioner and CBER Director, along with NIH and CDC leadership, have all met early with senior business and scientific officers of vaccine manufacturers to encourage initial steps and promise intense interaction in development of SARS vaccines

# SARS Vaccine Issues: Background

- Basic studies in viral pathogenesis and the natural history of the disease important for development & risk/benefit analyses of candidate vaccines.
- Safety evaluation necessary in appropriate animal systems prior to use/assessment in human clinical trials.
- Safety may be affected by many factors, e.g., the characteristics of the vaccine and the nature of protective immunity (e.g., need to estimate attenuation prior to initiation of clinical trials with a live-attenuated vaccine).

# SARS Vaccine: Major Issues

- Live attenuated vs. killed/component/recombinant
  - Potential concerns virulence/reversion vs. immunopathogenesis/efficacy
  - Killed vaccine likely fastest development pathway
- Defining protective antigen/variation & surrogates/durability of protection
- Determining safety & efficacy:
  - Animal models/immune surrogates as become known
  - Field trials likely needed to evaluate protection and for possible immunopathogenesis
  - LSTs should be feasible if epidemic continues
    - Special populations
  - IRB challenges in rapidly mobilizing SARS and other EID studies

# SARS Vaccine Actions

CBER facilitating SARS vaccine development by:

- Initiating collaborative studies to:
  - Develop assays required for vaccine characterization
  - Develop assays for evaluation of vaccine-induced immune responses
  - Determine degree of strain variation and sufficiency of protection of vaccine vs. natural strains
  - Evaluate animal models for vaccine safety and efficacy
- Providing guidance on:
  - Manufacturing concerns (e.g., up-front recommendations for cell banks, testing needed, etc.)
  - Use of animal models for vaccine evaluation (non-clinical safety and efficacy evaluations)
  - Clinical trial design

# Support Development of Therapeutic Drugs

- CDER worked with CDC to establish an emergency IND for IV Ribavirin (early in epidemic before questionable utility) if use of drug had been needed in U.S.
- Worked with USAMRID to identify potential candidates for sensitivity assay testing
- Worked with private sector to encourage ongoing submission of potential candidates to USAMRID for sensitivity assay testing
- Worked with NIH to design clinical protocols for use of potential candidates in clinical setting (if needed in U.S.)

# Biologics: Interferon α

- In vitro: coronavirus sensitive to human IFN-α
- Limited data suggests high dose prophylactic intranasal IFN may decrease infection rate
- No evidence re: IFN α given after exposure.
- Animal studies of systemic coronavirus infections suggest that IFN-α is ineffective therapy.
- Concern w/ IFN potentiation of cytokine injury

Conclusion: Intranasal IFN -α has potential prophylactic role, IFN α therapeutic role for systemic infection unlikely.

# Biologics: Antibodies as Therapeutics

- If protective epitopes identified Mabs, Pabs might offer potential as prophylaxis and possibly, though less likely, therapeutics
- Unlikely to be practical as prophylaxis
- Uncontrolled treatment use in Chinese outbreak
  - Potential for immune potentiation
  - If no antivirals, reasonable to perform contrrolled trials
  - Non-immune IGIV could be immunomodulatory
- Lower initial priority than vaccine, antivirals

# SARS & Blood Safety

- **CBER immediately began work with blood banking industry, private sector, NIH to investigate whether or not SARS potentially a blood/tissue borne disease**
- **April 17, 2003 issued guidance: Recommendations for the Assessment of Donor Suitability and Blood Product Safety in Cases of Suspected Severe Acute Respiratory Syndrome (SARS) or Exposure to SARS.**
- **Participated in joint WHO conferences to assess the SARS epidemic worldwide and to consider measures to safeguard the blood supply.**
  - **Provided input in the development of a WHO guidance on donor deferral**
- **Held public discussion at Blood Product Advisory Committee 6/03 about the epidemiology, pathogenesis of SARS agent and the Canadian experience**

# SARS & Blood Safety: continued

- **Facilitating development of possible donor screening tests:**
  - Participated in the FDA sponsored public workshop on "SARS Diagnostics: Scientific and Regulatory Challenges"
  - Working proactively with the manufacturers of diagnostic tests to determine possible extension to a blood screening indication
  - Collaborating with NIAID/NIH scientists to study the viremia of SARS-CoV agent in blood using animal models

# Other Regulatory Research Targeted to SARS

- Vaccine studies- immune markers/surrogates, Ags, models, vaccine delivery
- Evaluating active/passive immunity strategies
  - Studies of immune globulins to define which populations of antibody provide protection vs. those which may play a role in enhancing viral infection.
  - Determining which viral epitopes elicit antibody responses most effective for neutralization
- Multiplex nucleic acid microarray assay for SARS-CoV in blood and blood products
- Studies to determine methods for viral inactivation (collabs. W/ NIAID and NYBC): relevant to vaccine development & blood safety

# Adequacy of U.S. Medical Supplies

- Worked with Department and private sector to determine adequacy of U.S. medical supplies in case of a large SARS outbreak in the U.S. (supportive: ventilators, fluids, masks, etc.)

# Summary of FDA Actions

- **Assure safety and availability of existing products**
  - Blood and tissues
  - Medical care supplies
- **Facilitate development of needed new products**
  - Early and intense communication to:
    - Identify and publicize needs
    - Identify potential candidate approaches
    - Engage industry and government partners
    - Enhance availability of needed samples, reagents and seed stocks
  - Continuing high priority interaction/advice

# Product Development for Public Health when Markets Uncertain

You can at least try to lead a horse to water and make it drink!